

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460



OFFICE OF CHEMICAL SAFETY AND
POLLUTION PREVENTION

MEMORANDUM

DATE: April 17, 2020

SUBJECT: Zeta-Cypermethrin: Review of "Mechanical Dust Torsion: YT-1601 Dog Tag"

PC Code: 129064

Decision No.: 558845

Petition No.: NA

Assessment Type: Study Review

TXR No.: NA

MRID No.: 51036101

DP Barcode: D455844


Registration No.: 39039-14


Regulatory Action: Registration Review

Case No.: 2130

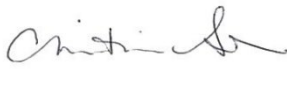
CAS No.: 97955-44-7

40 CFR: NA

From: Gerad Thornton, Chemist 
Risk Assessment Branch II
Health Effects Division (7509P)

Through: Wade Britton, MPH, Environmental Health Scientist 
Risk Assessment Branch IV
Health Effects Division (7509P)

And

Christina Swartz, Chief 
Risk Assessment Branch II
Health Effects Division (7509P)

To: Susan Bartow, Chemical Review Manager
Julie Javier, Team Leader
Linda Arrington, Branch Chief
Risk Management and Implementation Branch IV
Pesticide Re-Evaluation Division (7508P)

Introduction

The Pesticide Re-evaluation Division (PRD) requested that HED review a study titled "Mechanical Dust Torsion: YT-1601 Dog Tag" to support registration review of the insecticide zeta-cypermethrin. The study was reviewed by Versar, and the attached data evaluation record (DER) has been updated to reflect the Agency's conclusions. A protocol for the study was

reviewed by the Agency (D453649, M. Collantes, 9/16/2019), and there were no major issues identified with the proposed study design.

Purpose

During registration review, questions have been raised about the physical forms that are present on the surface of certain pet products such as collars and medallions. Under use conditions, active ingredients are removed from the surface of the product by contact with the dog or cat's hair coat through the activity of the animals. The Agency has been asking registrants to determine the amount of dust present on a collar, or that could be rubbed off of the product after mechanical stress. Torsion studies are conducted by exposing a product to mechanical torsion and stress by twisting and pulling the product multiple times to maximize potential release of solids. The torsion is meant to exaggerate the typical or expected movement of the product against the animal to release the active ingredients contained in its matrix. The exaggerated movement is done intentionally to generate what is assumed to be a theoretical maximum amount of dust.

Executive Summary

HED has evaluated the study “Mechanical Dust Torsion: YT-1601 Dog Tag” submitted by Y-TEX Corporation. The purpose of the study was to measure the amount of solids (dust/powder) released from a dog medallion and the active ingredient content of the released solids when the medallion is exposed to mechanical torsion and stress. The test product was YT-1601 Dog Medallion (EPA Reg No. 39039-14), containing 19.0% piperonyl butoxide and 10.5% zeta-cypermethrin/10.1% 4S-Isomer zeta-cypermethrin.

Three medallions were evaluated in the study. Each medallion was subjected to three torsion cycles, each consisting of ten twists, followed by gently tapping the sample into a pre-weighed pan. Each 8-g medallion was smoothly wiped with a Kimwipe (a low-linting wipe used in scientific laboratories) before the test and between torsion cycles. The medallions, Kimwipes, weigh pan, and gloves were weighed before and after the torsion test.

The Kimwipes were analyzed for piperonyl butoxide and zeta-cypermethrin using high performance liquid chromatography (HPLC) with UV Vis detection. The limit of quantitation (LOQ) was not reported. In addition, the Study Report did not provide any information regarding quality control samples, field blanks, or field recovery samples.

The Registrant and Versar calculated the amount of dust/powder removed from the medallions, the amount of dust/powder recovered on the collection matrices, and the percent of piperonyl butoxide and zeta-cypermethrin in the dust/powder collected.

The amount of dust/powder removed from the medallions, based on the weight difference before and after the torsion test, ranged from 0.005 g to 0.011 g (overall average of 0.008 g \pm 0.003 g). These values represent 0.06% to 0.14% of the initial weight of the medallions (overall average of 0.10% \pm 0.04%).

The following issues of concern are noted:

- Samples were analyzed for piperonyl butoxide and zeta-cypermethrin only and no discussion of production of metabolites or breakdown products was provided.
- The Study Report did not provide any information regarding quality control samples, field blanks, or field recovery samples.
- Storage stability data were not provided.
- The method LOQ and method validation data were not provided.

Conclusions

Despite the issues of concern noted above, HED has concluded that the quality of the study is sufficient that the results indicating a maximum of 0.14 % dust (average of 0.10 % dust) can be used quantitatively in HED's risk assessment for zeta-cypermethrin. These results are also generally consistent with the findings of similar studies for pet collars in general.

DATA EVALUATION RECORD

STUDY TYPE: Determination of Amount of Dust Generated from Mechanical Torsion of Pet Tag

TEST MATERIAL: The test material was an impregnated dog tag, referred to as YT-1601 Dog Medallion (EPA Registration Number 39039-14). The medallion contained 19.0% piperonyl butoxide and 10.5% zeta-cypermethrin/10.1% 4S-Isomer zeta-cypermethrin.

SYNONYMS: Zeta-cypermethrin; S-Cyano (3-phenoxyphenyl) methyl (\pm) cis/trans 3-(2,2-dichloroethenyl)-2,2 dimethylcyclopropane-carboxylate

Piperonyl Butoxide; 5-[2-(2-butoxyethoxy)ethoxymethyl]-6-propyl-1,3-benzodioxole

CITATION:

Study Author:	Mikel Walbridge
Title:	Mechanical Dust Torsion: YT-1601 Dog Tag
Report Date:	December 31, 2019
Performing Laboratory:	Y-TEX Corporation 1825 Big Horn Avenue Cody, Wyoming 82414 USA
Identifying Codes:	Y-TEX Study No. YT-1601-19-01; MRID 51036101

SPONSORS: Y-TEX Corporation
1825 Big Horn Avenue
Cody, Wyoming 82414

EXECUTIVE SUMMARY:

This report reviews the study “Mechanical Dust Torsion: YT-1601 Dog Tag” submitted by Y-TEX Corporation. The purpose of the study was to measure the amount of solids (dust/powder) released from a dog medallion and the active ingredient content of the released solids when the medallion is exposed to mechanical torsion and stress. The test product was YT-1601 Dog Medallion, containing 19.0% piperonyl butoxide and 10.5% zeta-cypermethrin/10.1% 4S-Isomer zeta-cypermethrin.

Three medallions were evaluated for this study. Each medallion was subjected to three torsion cycles, each consisting of ten twists, followed by gently tapping the sample into a pre-weighed pan. Each 8-g medallion was smoothly wiped with a Kimwipe before the test and between torsion cycles. The medallions, Kimwipes, weigh pan, and gloves were weighed before and after the torsion test.

The Kimwipes were analyzed for piperonyl butoxide and zeta-cypermethrin using high performance liquid chromatography (HPLC) with UV Vis detection. The limit of quantitation was not reported. In addition, the Study Report did not provide any information regarding quality control samples, field blanks, or field recovery samples.

The Registrant and Versar calculated the amount of dust/powder removed from the medallions, the amount of dust/powder recovered on the collection matrices, and the percent of piperonyl butoxide and zeta-cypermethrin in the dust/powder collected.

The amount of dust/powder removed from the medallions, based on the weight difference before and after the torsion test, ranged from 0.005 g to 0.011 g (overall average of $0.008 \text{ g} \pm 0.003 \text{ g}$). These values represent 0.06% to 0.14% of the initial weight of the medallions (overall average of $0.10\% \pm 0.04\%$).

Only the wipes showed an increase in post-test weight. The amount of dust/powder collected on the wipes after the torsion test ranged from 1.0 to 4.7 mg; the overall average was 2.3 mg. These values represent 15.3% to 41.2% of the amount of dust/powder removed from the medallions (overall average of $28.8\% \pm 13.8\%$) and 0.01% to 0.06% of the initial weight of the medallions (overall average of $0.03\% \pm 0.03\%$).

The Study reported that a total of 1.43 mg zeta-cypermethrin and 2.28 mg piperonyl butoxide were found in the three kimwipes; the average amount of residue per wipe was reported to be 0.49 mg zeta-cypermethrin and 0.76 mg piperonyl butoxide. The percent residue in the dust/powder collected in the tissues were 21.0% for zeta-cypermethrin and 33.5% for piperonyl butoxide. The percent residue transfer was 0.006% zeta-cypermethrin and 0.009% piperonyl butoxide based on the initial weight of the medallions or 0.058% zeta-cypermethrin and 0.049% piperonyl butoxide based on the initial dose applied.

The following issues of concern are noted:

- Samples were analyzed for piperonyl butoxide and zeta-cypermethrin only and no discussion of production of metabolites or breakdown products was provided.
- The Study Report did not provide any information regarding quality control samples, field blanks, or field recovery samples.
- Storage stability data were not provided.
- The method LOQ and method validation data were not provided.

COMPLIANCE: Signed and dated GLP, Quality Assurance, and Data Confidentiality statements were provided. The study sponsor waived claims of confidentiality within the scope of FIFRA Section 10(d) (1) (A), (B), or (C). The study sponsor stated that the study was conducted under EPA Good Laboratory Practice Standards (40 CFR part 160).

CONCURRENT EXPOSURE STUDY: No

WAS AIR SAMPLING CONDUCTED IN CONJUNCTION WITH SURFACE SAMPLING? No

GUIDELINE OR PROTOCOL FOLLOWED: The study was reviewed using applicable parts of the OPPTS Test Guidelines Series 875, Occupational and Residential Exposure Test Guidelines, Group B: 875.2100 (dislodgeable foliar residue), 875.2300 (indoor surface residue) and 875.2400 (dermal exposure). A compliance checklist is provided in Appendix A.

I. MATERIALS AND METHODS

A. MATERIALS

1. Test Material:

Active ingredients:	Zeta-cypermethrin and piperonyl butoxide
Formulation:	YT-1601 Dog Medallion, an impregnated dog tag containing 19.0% piperonyl butoxide and 10.5% zeta-cypermethrin/10.1 % 4S-Isomer zeta-cypermethrin.
Purity formulation:	The certificate of analysis states that the test product contained 19.0 % piperonyl butoxide (w/wt) and 10.1 % 4S-zeta-cypermethrin (w/w). Expiration date: not reported.
Lot # formulation:	EPM333711
CAS #(s):	Zeta-cypermethrin: 52315-07-8 Piperonyl Butoxide: 51-03-6
Other Relevant Information:	EPA Registration No. 39039-14

2. Relevance of Test Material to Proposed Formulation(s):

The test material appears to be the same as the product described on the label for YT-1601 Dog Tag (alternate brand names: Pest Shield, K9 Pest Shield, Pest Medallion, and K9 Pest Medallion), dated September 16, 2013 (EPA Registration No. 39039-14). YT-1601 Dog Tag contains a nominal 20.0% (wt/wt) piperonyl butoxide and 10% zeta-cypermethrin.

B. STUDY DESIGN

The study protocol, signed by the Study Director on December 16, 2019, was provided with the study report. There was one deviation from the protocol and no amendments. The deviation involved an incorrect reference to the CAS number for zeta-cypermethrin. Page 1 of the protocol referenced the incorrect CAS number for zeta-cypermethrin; the referenced CAS number was 979-44-7 and the correct CAS number is 52315-07-8.

- 1. Test location:** The study was conducted at Y-TEX Corporation in Cody, Wyoming.
- 2. Test System:** Three dog medallions, each weighing approximately 8 grams, were used in the study. Each medallion was subjected to three torsion cycles, each consisting of ten twists, followed by gently tapping the sample into a pre-weighed pan.

1. Physical State of Formulation as Applied:

The test substance was an impregnated dog medallion.

4. Torsion Test and Sampling Procedures:

- Method and Equipment: Medallions, tissue papers (KIMTECH kimwipes®), weigh pans, and cotton gloves were weighed before each mechanical torsion test.
- Sampling Procedure(s): Each 8-g medallion was smoothly wiped with a Kimwipe and the post-wipe weight was recorded. Each medallion sample was then subjected to three torsion cycles. A torsion cycle consisted of ten twists at 180° angles (or as close as practical), followed by gently tapping the sample into a pre-weighed weigh pan. The sample was smoothly wiped with a pre-weighed Kimwipe between torsion cycles. The same pre-weighed cotton glove was worn during sample preparation and through the torsion cycles.
- After the torsion cycles, the weights of the Kimwipe, weigh pan, glove, and medallion were recorded to nearest 0.0001 grams.
- Surface area sampled: Not reported.
- Sampling Time: Not reported.
- Replicates: Three medallions were sampled in this study.
- Times of sampling: Not applicable.

5. Sample Handling:

The Kimwipes were pooled and extracted and analyzed for zeta-cypermethrin and piperonyl butoxide. Storage conditions for the collection matrices were not reported.

6. Analytical Methodology:

- Extraction method(s): According to the analytical report, the Kimwipes were extracted with a 70:30 mixture of acetonitrile and water prior to analysis.
- Detection method(s): Analysis was performed using high performance liquid chromatography (HPLC) with UV Vis detection. Table 1 presents a summary of the typical operating conditions.

Table 1. Summary of Typical HPLC Operating Conditions		
%A:	95:5 Water:Methanol	
%C:	Acetonitrile	
Gradient:	Time	%C
	0	70.0
	3.5	100.0
	4.5	100.0
	5	70.0
	7	70.0
Column:	Kinetex 2.6 µm Polar C18 100Å, 100 X 3 mm	
Column Oven Temperature:	25 °C	
UV-Vis:	230 nm	

Table 1. Summary of Typical HPLC Operating Conditions

Injection Volume:	5 µL
-------------------	------

Method validation: Residues of zeta-cypermethrin and piperonyl butoxide on tissue matrices were determined using analytical method Y-TEX 1 MeCN Method V2. Method validation information was not provided.

The limit of quantitation was not reported.

Instrument performance and calibration: Not reported.

Quantification: Not reported.

8. Quality Control:

Lab Recovery/Field Blanks/Field Recovery: The Study Report did not provide any information regarding quality control samples, field blanks, or field recovery samples.

Formulation: The test product is an impregnated dog medallion containing 19.0% piperonyl butoxide and 10.5% zeta-cypermethrin/10.1% 4S-Isomer zeta-cypermethrin.

Tank mix: Not applicable.

Travel Recovery: The Study Report did not provide any information regarding travel recovery samples.

Storage Stability: Storage stability data were not provided.

II. RESULTS AND CALCULATIONS

The Registrant and Versar calculated the amount of dust/powder removed from the medallions, the amount of dust/powder recovered on the collection matrices, and the percent of piperonyl butoxide and zeta-cypermethrin in the dust/powder collected. The results (average and standard deviation) are shown in Tables 2-4.

As shown in Table 2, the amount of dust/powder removed from the medallions, based on the weight difference before and after the torsion test, ranged from 0.005 g to 0.011 g (overall average of 0.008 g \pm 0.003 g). These values represent 0.06% to 0.14% of the initial weight of the medallions (overall average of 0.10% \pm 0.04%).

Only the wipes showed an increase in post-test weight. The amount of dust/powder collected on the wipes after the torsion test ranged from 1.0 to 4.7 mg; the overall average was 2.3 mg. These values represent 15.3% to 41.2% of the amount of dust/powder removed from the medallions (overall average of 28.8% \pm 13.8%) and 0.01% to 0.06% of the initial weight of the medallion (overall average of 0.03% \pm 0.03%), as presented in Table 3.

The Study reported that a total of 1.43 mg zeta-cypermethrin and 2.28 mg piperonyl butoxide were found in the three kimwipes; the average amount of residue per wipe was reported to be 0.49 mg zeta-cypermethrin and 0.76 mg piperonyl butoxide. The percent residue in the dust/powder collected in the

tissues was 21.0% for zeta-cypermethrin and 33.5% for piperonyl butoxide. The percent residue transfer was 0.006% zeta-cypermethrin and 0.009% piperonyl butoxide based on the initial weight of the medallions or 0.058% zeta-cypermethrin and 0.049% piperonyl butoxide based on the initial dose applied.

III. DISCUSSION

A. LIMITATIONS OF THE STUDY:

The following issues of concern are noted:

- Samples were analyzed for piperonyl butoxide and zeta-cypermethrin only and no discussion of production of metabolites or breakdown products was provided.
- The Study Report did not provide any information regarding quality control samples, field blanks, or field recovery samples.
- Storage stability data were not provided.
- The method LOQ and method validation data were not provided.

B. CONCLUSIONS:

The Registrant and Versar calculated similar values for percent of dust/powder removed from the medallions, the percent of dust/powder recovered on the collection matrices, and the percent of piperonyl butoxide and zeta-cypermethrin in the dust/powder collected.

Table 2. Dust/Powder Removed from Medallions During Torsion Test				
Medallion No.	Initial weight (g)	Weight After Torsion Test (g)	Dust/Powder Removed from Medallion¹ (g)	% Dust/Powder Removed from Medallion²
1	8.1949	8.1835	0.0114	0.14%
2	8.1655	8.1605	0.0050	0.06%
3	8.1502	8.1430	0.0072	0.09%
Average			0.0079	0.10%
Standard deviation			0.0033	0.04%

1 Dust/powder removed from medallion = Medallion weight before torsion – Medallion weight after torsion

2 Percent of dust/powder removed = (Dust/powder removed from medallion / Medallion weight before torsion) x 100

Table 3. Dust/Powder Recovered on Collection Matrices During Torsion Test							
Medallion No.	Dust/Powder Removed from Medallion (g)	Dust/Powder Recovered on Collection Matrices (g)				% Dust/Powder Recovered on Collection Matrices³	% of Initial Weight Transferred⁴
		Glove¹	Tissue	Weigh Pan	Total²		
1	0.0114	-0.0030	0.0047	-0.0001	0.0047	41.2%	0.06%
2	0.0050	-0.0062	0.0010	0.0000	0.0010	20.0%	0.01%
3	0.0072	-0.0058	0.0011	0.0000	0.0011	15.3%	0.01%
Average					0.0023	28.8%	0.03%
Standard deviation					0.0021	13.8%	0.03%

1 The Study Report noted that the gloves lost an average of 5 mg in each replicate despite being rinsed in acetone and allowed to dry prior to the experiment.

2 Include the weights of the tissues only. For the glove and weigh pan matrices, the weight after the torsion test was less than initial weight; it was assumed that there was no weight gain, so the amount of dust/powder recovered was set to zero.

3 Percent dust/powder recovered = (Dust/powder collected on tissues / Dust/powder removed from medallion) x 100

3 Percent of initial weight transferred = (Dust/powder collected on tissues / Initial weight of medallion) x 100.

Table 4. Percent Residue Transfer During Torsion Test		
	Piperonyl Butoxide	Zeta-cypermethrin
Percent Residue in Dust/Powder Collected (Tissues)		
Total Weight of Dust/Powder on Tissues (mg)	6.8	6.8
Amount ai in tissue (mg)	2.28	1.43
Percent ai (%)	33.5	21.0
Percent Residue of Initial Weight		
Total Weight of Medallions (mg)	24510.6	24510.6
Amount ai in tissue (mg)	2.28	1.43
Percent ai (%)	0.009	0.006
Percent Residue of Applied Dose¹		
Total Dose Applied (mg)	4657.0	2475.6
Amount ai in tissue (mg)	2.28	1.43
Percent ai (%)	0.049	0.058

¹ Applied dose = Initial weight of medallion x % ai, where % ai is 10.1% for zeta-cypermethrin and 19.0% for piperonyl butoxide

Appendix A

Compliance Checklist

COMPLIANCE CHECKLIST

This compliance checklist is based on applicable criteria of the OPPTS Test Guidelines Series 875, Occupational and Residential Exposure Test Guidelines, Group B: 875.2300 (indoor surface residue) and OPPTS Test Guidelines Series 875, Occupational and Residential Exposure Test Guidelines, Group B: 875.2400 (dermal exposure).

1. *The test substance must be the typical end use product of the active ingredient.* This criterion was met.
2. *The production of metabolites, breakdown products, or the presence of contaminants of potential toxicologic concern, should be considered on a case-by-case basis.* It is uncertain if this criterion was met. Samples were analyzed for piperonyl butoxide and zeta-cypermethrin only and no discussion of production of metabolites or breakdown products was provided.
3. *Indoor surface residue studies should be conducted under ambient conditions similar to those encountered during the intended use season, and should represent reasonable worst case conditions.* This criterion does not apply.
4. *Ambient conditions (i.e., temperature, barometric pressure, ventilation) should be monitored.* This criterion does not apply.
5. *The end use product should be applied by the application method recommended on the label.* This criterion does not apply.
6. *The application rate used in the study should be provided and should be the maximum rate specified on the label. However, monitoring following application at a typical application rate is more appropriate in certain cases.* This criterion does not apply.
7. *If multiple applications are made, the minimum allowable interval between applications should be used.* This criterion does not apply. Only one application was made.
8. *Indoor surface residue (ISR) data should be collected from several different types of media (e.g., carpeting, hard surface flooring, counter tops, or other relevant materials).* This criterion does not apply.
9. *Sampling should be sufficient to characterize the dissipation mechanisms of the compound (e.g., three half-lives or 72 hours after application, unless the compound has been found to fully dissipate in less time; for more persistent pesticides, longer sampling periods may be necessary). Sampling intervals may be relatively short in the beginning and lengthen as the study progresses. Background samples should be collected before application of the test substance occurs.* This criterion does not apply.
10. *Triplicate, randomly collected samples should be collected at each sampling interval for each surface type.* This criterion was met. Three medallions were sampled.
11. *Samples should be collected using a suitable methodology (e.g., California Cloth Roller, Polyurethane Roller, Drag Sled, Coupons, Wipe Samples, Hand Press, vacuum cleaners for dust and debris, etc.) for indoor surfaces.* This criterion appears to be met. Samples were collected using lint-free cloths and cotton gloves.

12. *Samples should be stored in a manner that will minimize deterioration and loss of analytes between collection and analysis. Information on storage stability should be provided.* This criterion was not met. Information on storage stability was not provided.
13. *Validated analytical methods of sufficient sensitivity are needed. Information on method efficiency (residue recovery), and limit of quantitation (LOQ) should be provided.* This criterion was not met. The LOQ and method validation data were not provided.
14. *Information on recovery samples must be included in the Study Report. A complete set of field recoveries should consist of at least one blank control sample and three or more each of a low-level and high-level fortification. These fortifications should be in the range of anticipated residue levels in the field study.* This criterion was not met. The Study Report did not provide any information regarding field recovery samples.
15. *Raw residue data must be corrected for appropriate recovery values.* This criterion was not met. The Study Report did not provide any information regarding quality control samples or field recovery samples.
16. *The monitoring period should be of sufficient duration to result in reasonable detectability on dosimeters. Monitoring should be conducted before residues have dissipated beyond the limit of quantification. Baseline samples should be collected before the exposure activity commences.* These criteria do not apply.
17. *Activities monitored must be clearly defined and representative of typical practice.* Each medallion was exposed to three mechanical torsion cycles, each consisting of ten twists, to simulate the normal release of dust/powder (and active ingredients) from the medallion.
18. *Sufficient control samples should be collected.* This criterion was not met. The Study Report did not provide any information regarding quality control samples or field blanks.